

## Early investigations into improving bowel and bladder function in fetal ovine myelomeningocele repair.

**Journal:** J Pediatr Surg

**Publication Year:** 2022

**Authors:** Christina M Theodorou, Jordan E Jackson, Sarah C Stokes, Christopher D Pivetti, Priyadarsini Kumar, Zachary J Paxton, Karen E Matsukuma, Kaeli J Yamashiro, Lizette Reynaga, Alicia A Hyllen, Arthur J de Lorimier, Maheen Hassan, Aijun Wang, Diana L Farmer, Payam Saadai

**PubMed link:** 35093254

**Funding Grants:** Placental Stem Cells for the In Utero Treatment of Spina Bifida , Placental Mesenchymal Stem Cell Augmentation of Fetal Myelomeningocele Repair, The CuRe Trial: Cellular Therapy for In Utero Myelomeningocele Repair

### Public Summary:

Myelomeningocele (MMC), the most severe form of spina bifida, results from incomplete closure of the spinal canal during development. The physical and chemical trauma resulting from exposure of the fetal spinal cord causes impaired lower extremity, bowel and bladder function. Results from our research studies demonstrate in utero MMC repair with placental derived mesenchymal stem cells (PMSCs) seeded on an extracellular matrix (ECM) "like" patch significantly improved lower extremity function in a sheep model. The ability of PMSCs to differentiate into many cell types have been utilized in disease treatment applications for tissue re-growth and new blood vessel formation. In this study, we hypothesized PMSCs seeded on an extracellular matrix (PMSC-ECM) patch will greatly improve bowel and bladder function in the lamb model. The patch was made to mimic the ECM, a network of proteins and compounds that surrounds cells, to match the local fetal spine microenvironment. MMC defects were surgically created in twelve sheep fetuses at gestational age (GA) 73 days, and subsequently repaired with PMSC-ECM at GA 101 days. Bowel and bladder function was evaluated using three methods: resting anal pressure, rectoanal inhibitory reflex (RAIR) presence, and rectal and bladder muscle thickness. Resting anal pressures and rectal and bladder muscle thickness was consistent among repaired MMC lambs and controls. Additionally, RAIR was observed in 3/5 repaired MMC lambs. These results indicate sheep fetal MMC repair treated with PMSC-ECM results in near-normal bowel and bladder function. However, further studies are needed to evaluate the efficacy of this treatment in human patients.

### Scientific Abstract:

**INTRODUCTION:** Fetal myelomeningocele (MMC) repair improves lower extremity motor function. We have previously demonstrated that augmentation of fetal MMC repair with placental mesenchymal stromal cells (PMSCs) seeded on extracellular matrix (PMSC-ECM) further improves motor function in the ovine model. However, little progress has been made in improving bowel and bladder function, with many patients suffering from neurogenic bowel and bladder. We hypothesized that fetal MMC repair with PMSC-ECM would also improve bowel and bladder function. **METHODS:** MMC defects were surgically created in twelve ovine fetuses at median gestational age (GA) 73 days, followed by defect repair at GA101 with PMSC-ECM. Fetuses were delivered at GA141. Primary bladder function outcomes were voiding posture and void volumes. Primary bowel function outcome was anorectal manometry findings including resting anal pressure and presence of rectoanal inhibitory reflex (RAIR). Secondary outcomes were anorectal and bladder detrusor muscle thickness. PMSC-ECM lambs were compared to normal lambs (n = 3). **RESULTS:** Eighty percent of PMSC-ECM lambs displayed normal voiding posture compared to 100% of normal lambs (p = 1). Void volumes were similar (PMSC-ECM 6.1 mL/kg vs. normal 8.8 mL/kg, p = 0.4). Resting mean anal pressures were similar between cohorts (27.0 mmHg PMSC-ECM vs. normal 23.5 mmHg, p = 0.57). RAIR was present in 3/5 PMSC-ECM lambs that underwent anorectal manometry and all normal lambs (p = 0.46). Thicknesses of anal sphincter complex, rectal wall muscles, and bladder detrusor muscles were similar between cohorts. **CONCLUSION:** Ovine fetal MMC repair augmented with PMSC-ECM results in near-normal bowel and bladder function. Further work is needed to evaluate these outcomes in human patients.